

CLAIMS

1. Use of an organic compound comprising an aromatic ring, noted Ar, substituted with at least one hydrocarbon substituent noted A, said hydrocarbon substituent comprising:
- a nonfunctionalized linear aliphatic chain noted $-CH_2A'$ comprising at least one carbon atom, and
 - a substituent noted F_a comprising at least one proton donor or acceptor function capable of establishing one or more hydrogen bonds,
 - in order to bring about the allosteric inhibition of the Tat protein.
2. Use according to claim 1, characterized in that the aromatic ring Ar is a derivative of toluene or a condensed polycyclic aromatic hydrocarbon.
3. Use according to claim 2, characterized in that the aromatic ring Ar is chosen from naphthalene, anthracene, phenanthrene, fluoranthene, aceanthrylene and triphenene.
4. Use according to claim 3, characterized in that the aromatic ring is a triphenene.
5. Use according to one of claims 1 to 4, characterized in that the aromatic ring interacts with tryptophan No. 11 of the Tat protein,, and with phenylalanine No. 38 of the Tat protein.
6. Use according to one of the preceding claims, characterized in that the substituent F_a establishes one or more hydrogen bonds with the basic region of the Tat protein and the N-terminal region of Tat.
7. Use according to one of the preceding claims, characterized in that the proton donor or acceptor function of the substituent F_a is situated at a distance of between 5 and 10 Å from the aromatic ring.
8. Use according to claim 7, characterized in that the proton donor or acceptor function of the substituent F_a is situated at a distance of between 6 and 7 Å from the aromatic ring.

9. Use according to one of the preceding claims, characterized in that the nonfunctionalized linear aliphatic chain $-CH_2A'$ comprises 1 to 8 atoms, among which carbon atoms and optionally one or two
5 heteroatoms.

10. Use according to claim 9, characterized in that the nonfunctionalized linear aliphatic chain $-CH_2A'$ comprises a carbon atom and F_a represents a hydroxyl, such that A represents $-CH_2OH$.

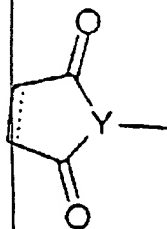
10 11. Use according to claim 9, characterized in that the nonfunctionalized linear aliphatic chain $-CH_2A'$ comprises 5 carbon atoms.

12. Use according to one of the preceding claims, with the exception of claim 10, characterized in that
15 the substituent F_a comprises at least two proton acceptor functions.

13. Use according to claim 12, characterized in that the substituent F_a comprises at least two proton acceptor functions situated in the plane of the
20 aromatic ring and on the same side of the plane of the aromatic ring.

14. Use according to claim 12 or 13, characterized in that the proton acceptor function is a carbonyl.

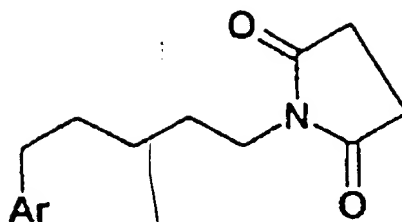
15. Use according to claim 14, characterized in
25 that the substituent F_a corresponds to the formula:



in which Y represents N or CH and the dotted line represents a possible double bond.

16. Use according to claim 15, characterized in
30 that the substituent F_a is a maleimide or is succinimide.

17. Use according to claim 16, characterized in that the compound corresponds to the formula:



18. Use according to Claim 17, characterized in that Ar represents triphenyl.

19. Use according to one of the preceding claims, characterized in that the aromatic ring Ar substituted with A comprises in addition at least one other substituent noted B or C, it being possible for the said substituent to comprise at least one carbon atom, and to comprise a substituent noted F_b or F_c comprising at least one proton donor or acceptor function capable of establishing one or more hydrogen bond with the Tat protein.

20. Use according to claim 19, characterized in that the aromatic ring comprises two other aliphatic substituents noted B and C.

21. Use according to claim 19 or 20, characterized in that B or C represents a methyl.

22. Use according to claim 19 or 20, characterized in that B or C comprises at least one proton donor or acceptor function.

23. Use according to claim 23, characterized in that B or C represents -COOH.

24. Use according to claim 23, characterized in that B or C comprises at least one hydroxyl function.

25. Use according to claim 24, characterized in that B or C represents -CH₂OH.

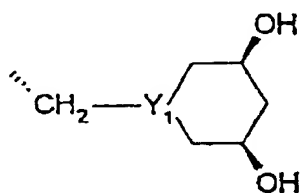
26. Use according to claim 23, characterized in that B or C comprises two proton donor or acceptor functions situated

- in the plane of the aromatic ring, or
- on the same side of the plane of the aromatic ring.

27. Use according to one of claims 18 to 26, characterized in that the organic compound corresponds to the formula

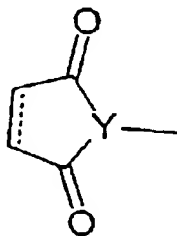
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15 in which Y1 represents N (compound noted TDS2), or
CH (compound noted TDS3).

28. Derivatives of triphenyl substituted with a
hydrocarbon substituent A comprising a
nonfunctionalized linear aliphatic chain and, at the
end of this chain, a substituent corresponding to the
20 formula:



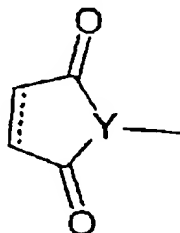
in which Y represents N or CH and the dotted line
represents a possible double bond.

29. Derivatives according to claim 28,
25 characterized in that the hydrocarbon group is a
maleimide or a succinimide.

30. Derivatives according to claim 28 or 29,
characterized in that the nonfunctionalized linear
chain comprises up to 8 atoms.

31. Di- or trisubstituted derivatives of triphenene comprising

- a hydrocarbon substituent A comprising a nonfunctionalized linear aliphatic chain and, at the end of this chain, a substituent corresponding to the formula,



in which Y represents N or CH and the dotted line represents a possible double bond.

and

- at least one second substituent B or C.

32. Derivatives according to claim 31, characterized in that the linear aliphatic chain of A comprises up to 8 atoms, among which are carbon atoms and optionally one or two heteroatoms.

33. Derivatives according to claim 32, characterized in that the linear aliphatic chain of A comprises 5 atoms.

34. Derivatives according to one of claims 31 to 33, characterized in that B and/or C are, independently of each other, aliphatic substituents comprising 1 to 4 carbon atoms.

35. Derivatives according to claim 34, characterized in that B and C represent a methyl.

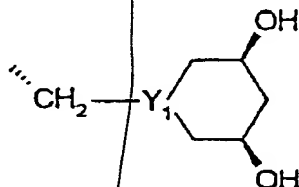
36. Derivatives according to claims 31 to 34, characterized in that B and/or C are, independently of each other, provided with at least one proton donor or acceptor function.

37. Derivatives according to claim 36, characterized in that B and C represent $-CH_2OH$.

38. Derivatives according to claim 36, characterized in that B and/or C are, independently of each other, provided with two proton donor or acceptor

functions arranged in space such that the functions are situated

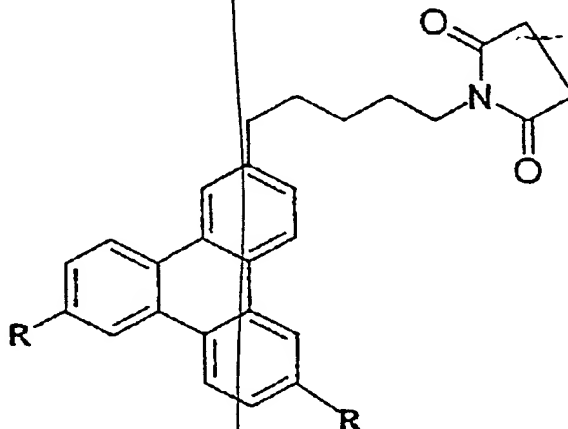
- in the plane of the triphenene nucleus or
- on the same side of the plane of the triphenene nucleus.



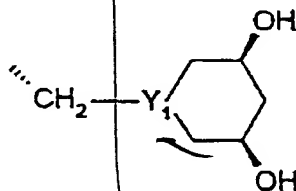
39. Derivatives according to claim 38, characterized in that B and C are identical and each represent:

10 Y1 being a nitrogen atom or a CH group.

40. Derivatives according to one of claims 31 to 39, of formula:



15 in which R represents a methyl (compound noted TDS1),
-CH₂OH (compound noted TDS4), or
the group of formula



in which Y1 represents N (compound noted TDS2),
or CH (compound noted TDS3).

20 41. 2,6,10-Trihydroxymethyltriphenene and 2,6,10-tricarboxytriphenene.

42. Method of preparing one of the trisubstituted compounds $\text{Ar}(\text{ABC})$ according to claims 31 to 40 such that A (noted $\text{CH}_2\text{-A}'\text{F}_a$) comprises a nonfunctionalized linear aliphatic chain ($\text{CH}_2\text{-A}'$), substituted at its end with a group provided with at least one proton acceptor or donor function (F_a), characterized in that it uses as intermediate product a derivative of formula $\text{P}_a\text{A}'\text{-H}_2\text{C-Ar-(CH}_2\text{Z)}_2$ in which $\text{-CH}_2\text{A}'$ is as defined above, P_a represents a hydrolyzable protective group and Z represents a hydrogen, a halogen or a protected alcohol function.

43. Method according to claim 42, characterized in that Z is a bromine or a trialkylsilyloxy group.

44. Method according to either of claims 42 or 43, characterized in that it uses $\text{Ar}(\text{CH}_3)_3$ as starting material.

45. Method according to one of claims 42 to 44, characterized in that it comprises the following successive steps:

- (a) attachment of the nonfunctionalized linear aliphatic chain $\text{-CH}_2\text{A}'$,
- (b) possible attachment of the substituents B and C, and
- (c) attachment of a substituent comprising at least one proton acceptor or donor function F_a to the nonfunctionalized chain $\text{-CH}_2\text{A}'$.

46. Method according to one of claims 42 to 45, characterized in that the derivative $\text{P}_a\text{A}'\text{-H}_2\text{C-Ar-(CH}_2\text{Z)}_2$ is obtained by magnesian synthesis, using the compound of formula $\text{P}_a\text{A}'\text{-MgX}^1$, in which X^1 is a halogen atom, $\text{P}_a\text{A-MgX}^1$ being for example $\text{BnO-(CH}_2\text{)}_n\text{-MgBr}$, n being greater than 1, and Bn representing a benzyl.

47. Method according to one of claims 42 to 46, characterized in that the compounds $\text{Ar}(\text{ABC})$ are such that B and C represent a methyl, and in that the monohalogenation of $\text{Ar}(\text{Me})_3$ is carried out in order to obtain $(\text{X}^2\text{-H}_2\text{C})\text{-Ar-(Me)}_2$, X^2 representing a halogen.

48. Method according to one of claims 42 to 46, characterized in that the compounds $\text{Ar}(\text{ABC})$ are such that the groups B and C each comprise at least one proton acceptor or donor function (F_b and F_c), and such that the bonds established by F_b and F_c with $\text{A-Ar}-(\text{CH}_2-)_2$ are carbon-carbon bonds, and in that the intermediate $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ is such that Z represents a protected alcohol function or a halogen.

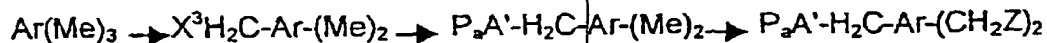
49. Method according to claim 48, characterized in that when Z represents a halogen, a ylide derived from $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ is reacted with a ketone comprising at least one proton donor or acceptor function F_b and/or F_c .

50. Method according to claim 49, characterized in that the ylide derived from $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ is obtained directly from $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ or via $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{SO}_2\text{Ph})_2$.

51. Method according to claim 48, characterized in that when Z represents a protected alcohol function, an aldehyde obtained by oxidation of $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ is exposed to ylide precursors of F_b and F_c .

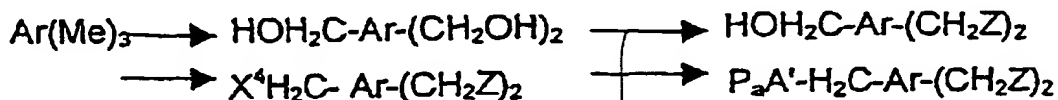
52. Method according to one of claims 42 to 46, characterized in that the compounds $\text{Ar}(\text{ABC})$ are such that the groups B and C each comprise at least one proton acceptor or donor function (F_b and F_c), and such that the bonds established by F_b and F_c with $\text{A-Ar}-(\text{CH}_2-)_2$ are carbon-nitrogen bonds, and in that the intermediate $\text{P}_a\text{A}'-\text{H}_2\text{C-Ar}-(\text{CH}_2\text{Z})_2$ is such that Z represents a halogen or a protected alcohol function.

53. Method according to claim 52, characterized in that Z represents a halogen and in that it comprises the following steps:



X^3 representing a halogen.

54. Method according to 52, characterized in that Z represents a protected alcohol function and step (a) follows the following scheme



X^4 representing a halogen.

55. Method according to 53, characterized in that the compound $\text{P}_a\text{A}'\text{-H}_2\text{C-Ar-(CH}_2\text{Z)}_2$ such that Z represents a halogen is reacted with a compound of the secondary amine type comprising at least one proton donor or acceptor function F_b and/or F_c .

56. Method according to one of claims 42 to 46, characterized in that the compounds Ar(ABC) are such that the groups B and C each comprise at least one proton acceptor or donor function (F_b and F_c), and such that the bonds established by F_b and F_c with $\text{A-Ar-(CH}_2\text{-)}_2$ are carbon-oxygen bonds, and in that the intermediate $\text{P}_a\text{A}'\text{-H}_2\text{C-Ar-(CH}_2\text{Z)}_2$ is such that Z represents a protected alcohol function.

57. Method according to claim 56, characterized in that when B and C represent CH_2OH , F_b and F_c represent OH and step (b) consists in deprotecting the alcohol function of $\text{P}_a\text{A}'\text{-H}_2\text{C-Ar-(CH}_2\text{Z)}_2$.

58. Method according to one of claims 45 to 57, characterized in that when F_a represents a maleimide or a succinimide, step (c) follows the conditions of the Mitsunobu reaction.

59. Method according to one of claims 45 to 58, characterized in that the aromatic nucleus is a triphenene.

60. Compounds according to one of claims 1 to 41, which are capable of being obtained by the method of one of claims 49 to 66 for their application as therapeutically active substances.

61. Compounds according to claim 60, as anti-retroviral agents for the treatment or the prevention of infections due to a retrovirus, in particular HIV.

62. Pharmaceutical preparations containing a compound according to claims 60 or 61, and a pharmaceutically inert excipient.

63. Pharmaceutical preparations according to claim
62, containing a mixture of a compound according to
claim 61 and of another anti-retroviral agent, as
combination product for use simultaneously, separately
5 or spaced out over time, in an anti-retroviral therapy.